
Repair and regeneration of tracheal surface epithelium and submucosal glands in a mouse model of hypoxic-ischemic injury.

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Public Summary:

Here we used a mouse model of airway injury to develop a temporal and spatial map of airway repair and regeneration. We defined the cell types that regenerate at specific stages. By increasing our understanding of the process by which airway repair occurs we hope to develop new therapies for airway diseases.

Scientific Abstract:

Background and objective: The heterotopic syngeneic tracheal transplant mouse model is an acute hypoxic-ischemic injury model that undergoes complete repair and regeneration. We hypothesized that the repair and regeneration process of the surface epithelium and submucosal glands would occur in a reproducible pattern that could be followed by the expression of specific markers of epithelial cell types. Methods: We used the syngeneic heterotopic tracheal transplant model to develop a temporal and spatial map of cellular repair and regeneration by examining the tracheal grafts at post-transplant days 1, 3, 5, 7, 10 and 14. We used pulsed BrdU and immunofluorescent staining to identify and follow proliferating and repairing cell populations. Results: We confirmed the reproducibility of the injury and repair in the model and we found a distinct sequence of reappearance of the various stem/progenitor and differentiated cell populations of the tracheal surface epithelium and submucosal glands. In the initial phase, the basal and duct cells that survived the injury proliferated to re-epithelialize the basement membrane with K5 and K14 expressing cells. Then these cells proliferated further and differentiated to restore the function of the epithelium. During this repair process, TROP-2 marked all repairing submucosal gland tubules and ducts. Non-CCSP-expressing serous cells were found to differentiate 4-5 days before Clara, mucus and ciliated cells. Conclusions: Improving our understanding of the reparative process of the airway epithelium will allow us to identify cell-specific mechanisms of repair that could be used as novel therapeutic approaches for abnormal repair leading to airway diseases.

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